

# Thyroid Scintigraphy

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## Warning:

The intravenous administration of sodium perchlorate mentioned in this recommendation is a non-registered application.

## 1. Introduction

Follicular cells of the thyroid are capable of clearing iodine, in the form of iodide, from the blood by active uptake ('trapping'). Uptake occurs via the sodium iodide-symporter (NIS), a transporter protein located on the basal membrane of thyroid epithelial cells. After uptake in the cell, the iodine is organically bound (organification). In this process, iodide (I<sup>-</sup>) is oxidized to I<sup>+</sup> under the influence of thyroid peroxidase (TPO). Then the I<sup>+</sup> is incorporated into tyrosyl-residues of thyroglobulin molecules to become mono- en di-iodotyrosine (MIT and DIT), and these tyrosines are joined to become tri- en tetraiodothyronine (the thyroid hormones T3 and T4). Only thyroid cells are capable of both trapping and organification of iodine. The pertechnetate ion (TcO<sub>4</sub><sup>-</sup>) has the same charge as the I<sup>-</sup> ion and also has similar dimensions. Like iodide, it is taken up into the thyroid epithelial cell through the NIS, which makes scintigraphy of the uptake process possible with <sup>99m</sup>Tc-pertechnetate. However, pertechnetate is not organified. Diagnostic imaging of the organification function can therefore only be accomplished with an iodine radionuclide; <sup>123</sup>I-sodium iodide is recommended for this.

## 2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

## 3. Indications

- a. Differentiation of the cause of thyrotoxicosis based on an increased or decreased uptake of the radiopharmaceutical, be it diffuse or (multi)focal.
- b. Determination of the function of palpable thyroid abnormalities (diffuse goitre, multinodular goitre, solitary nodule: cold/hot/indifferent), so as to gain an impression of the nature of the abnormalities.
- c. Determination of the functional mass of the thyroid, inter alia for purposes of dose calculation in <sup>131</sup>I-therapy.
- d. Determination of the size and extent (e.g. retrosternally) of a goitre.
- e. Demonstration or exclusion of ectopic thyroid tissue (e.g. to differentiate a median neck cyst or a rudimentary ductus thyroglossus).
- f. Differential diagnosis of congenital hypothyroidism (agenesis, impaired descensus, dysmorphogenesis).

#### 4. Contraindications.

- a. *Lactation.* Breast feeding should be interrupted for at least 3 weeks, when using  $^{123}\text{I}$  according to IRCP 106. When using  $^{99\text{m}}\text{Tc}$  pertechnetate breast feeding should be interrupted for 12 h.
- b. *Pregnancy.* Treatment with  $^{131}\text{I}$  is absolutely contraindicated in pregnancy. When scintigraphy is requested in preparation for such treatment, this is likewise contraindicated. Differentiating causes of thyrotoxicosis can usually be postponed until after pregnancy.

#### 5. Relation to other diagnostic procedures

- a. In principle, the scintigraphic method is insufficient for measuring thyroid volume in order to calculate the  $^{131}\text{I}$  dose required for treatment of Graves' disease (see " $^{131}\text{I}$  therapy in primary hyperthyroidism and non-toxic (multi)nodular goitre."). The average measurement error is approximately 30%. Ultrasound is the method of choice. For the calculation of the (functional) volume in other forms of thyroid disease, scintigraphy is sufficient, especially in combination with accurate palpation. If uncertainty exists about the extent of retrosternal extension of a goitre, this may be determined either by CT (without contrast) or MRI. The request form should then specifically indicate that a volume calculation is required.
- b. Ultrasound (following TSH assay) is better than scintigraphy for the analysis of a solitary nodule. The supplementary diagnostics are completed with a fine needle aspiration biopsy (FNA) whenever the TSH is not suppressed. If the TSH is suppressed, thyroid scintigraphy is indicated to determine the presence/ absence of an autonomous nodule.

#### 6. Medical information necessary for planning

- a. Clinical considerations and findings on palpation.
- b. Thyroid function tests results (TSH, Free T4 and possibly Free T3).
- c. Medication.
- d. Results of other relevant investigations (e.g. ultrasound, tracheal imaging, previous scintigraphy).
- e. Pregnancy and lactation excluded

#### 7. Radiopharmaceutical

Preparation:  $^{99\text{m}}\text{Tc}$ -sodium pertechnetate (pump function), or  $^{123}\text{I}$ -sodium iodide (pump function and organification)

Nuclide: Technetium-99m or Iodine-123

Activity:  $^{99\text{m}}\text{Tc}$ : 80-180 MBq,  $^{123}\text{I}$ : 10-20 MBq (neonates 3 MBq)

Administration: Intravenous; for investigation of the organification function  $^{123}\text{I}$ -iodide can also be administered orally

#### 8. Radiation safety

As stated above, pregnancy and lactation are absolute contraindications for  $^{131}\text{I}$  therapy.

Also see: The SNMMI practice guideline for treatment of thyroid disease with  $^{131}\text{I}$  3.0 (JNM 2012).

**Radiation Dosimetry for Adults**

<b>Radiopharmaceutical</b>	<b>Administered Activity MBq</b>	<b>Organ Receiving The Largest Radiation Dose mGy/MBq</b>	<b>Effective Dose Equivalent mSv/MBq</b>
Na <sup>123</sup> I iodide*	7,5 - 25 p.o.	Thyroid 3,2	0,11
<sup>99m</sup> Tc pertechnetate	75 - 370 i.v.	ULI** 0,062	0,013
Na <sup>131</sup> I-iodide*	1,85 - 3,7 p.o.	Thyroid 360	11

\*assuming 25% uptake

\*\*ULI-upper large intestine

**Radiation Dosimetry for Children (5 years old)**

<b>Radiofarmaceutical</b>	<b>Administered Activity (MBq/ Kg)</b>	<b>Organ Receiving The Largest Radiation Dose mGy/MBq</b>	<b>Effective Dose Equivalent mSv/MBq</b>
Na <sup>123</sup> I iodide*	0,1 – 0,3 p.o.	Thyroid 16	0,54
<sup>99m</sup> Tc pertechnetate	1,8 – 9,2 i.v.	ULI** 0,21	0,04

\*assuming 25% uptake

\*\*ULI-upper large intestine

**9. Patient preparation/essentials for procedure**

- The use of thyrostatics or combination therapy (thyrostatics plus levothyroxine) should be stopped 3 days prior to the investigation. Monotherapy with Propylthiouracil should be stopped for at least 15 days; monotherapy with levothyroxine should be stopped 4 weeks in advance. Alternatively, a suppressed TSH can be chosen as the standard condition.
- Just before thyroid gland scintigraphy, allow the patient to drink water to remove the activity of the saliva from the oesophagus.
- Ensure the patient has not received large doses of iodine recently. For example in

the form of x-ray/CT contrast media, iodinated drugs (amiodarone, cough syrups), cosmetics (povidone soap and shampoo), kelp tablets and other seaweed preparations. After such an iodine load, thyroid gland uptake of iodine, pertechnetate (and perchlorate) will be disturbed for 3 weeks to 6 months, depending on the amount of iodine received. Gadolinium-DTPA (MRI contrast medium) does not interfere with thyroid uptake of iodine.

*Essentials for the procedure*

- a. Point source.
- b. Size marking (using pinhole collimator).
- c. For  $^{123}\text{I}$  scintigraphy in suspected hormone synthesis disorder: 1 ampoule of sodium perchlorate.

**10. Acquisition and processing**

Gamma camera and computer

*Technetium scintigraphy*

Energy:  $^{99\text{m}}\text{Tc}$ -setting, 140 keV

Window: 15-20%

Collimator: LEAP or pinhole collimator

LEAP: if possible use the zoom factor for optimal resolution

Pinhole: if using a pinhole collimator, the variable magnification factor must be taken into account. Therefore, always use a fixed distance between the pinhole and neck. The pinhole collimator has the added disadvantage that retrosternal extension and/or ectopic thyroid tissue can be missed (due to the limited visibility)

Counting time: 350.000 counts or maximally 10 min per view

Matrix size: 128×128

*Iodine scintigraphy*

Energy:  $^{123}\text{I}$ -setting, 159 keV

Window: 15-20%

Collimator: LEAP- or pinhole-collimator (see remarks under Technetium scintigraphy). Some prefer a (medium energy) ME collimator

Counting time: 350.000 counts or maximally 10 min per view

Matrix size: 128×128

Procedure

- a. *Palpation*: prior to scintigraphy, the neck is palpated and palpation findings recorded. During scintigraphy the suprasternal notch and any palpable abnormalities are indicated in a separate recording using a point source.
- b. *Technetium scintigraphy* may be performed as of 15 to 20 min post intravenous injection.

For adequate assessment of the organification function of the thyroid, the iodine scintigraphy must be done no less than 2 h after oral or intravenous administration of  $^{123}\text{I}$ . When including a 'wash-out test' on suspicion of congenital hypothyroidism, an interval of 4 h is used; this is due to the standardisation of the assessment criteria for

pathological wash-out.

- c. *Views:* anterior (preferably lying down; if sitting, adequate fixation is required). In the event of uncertainty, and in case of cold nodules, 30°-45° anterior oblique recordings can be made in addition to the standard views.
- d. *Size determination:* this is done most simply and accurately with the LEAP collimator by starting from the (known) pixel size in the acquisition parameters used. When using a pinhole collimator for size determination, two markers separated by a known distance are needed. Since the magnification factor of a pinhole collimator is not the same for all parts of the thyroid, a parallel-hole collimator is preferred for volume estimates.
- e. *Iodine absorption rate measurement:* this can be performed with the gamma camera. Following on from the imaging of the neck and with the same image acquisition parameters, a recording is made of an <sup>123</sup>I source of known strength placed in a neck phantom. From this, the number of counts per MBq is derived and the data is used to calculate the percentage of the dose administered to the patient which is taken up by the thyroid.
- f. In *congenital hypothyroidism*, the investigation is conducted 4 h after administration of <sup>123</sup>I-sodium iodide (neonatal dose: 3 MBq). Both anterior and lateral recordings are made. Use of a "flood-field" activity source simplifies the anatomical localization. Marking the place where iodine uptake is visualized (using a point source) is recommended. If iodine uptake is observed in the thyroid gland, this is followed by a "wash-out-test" performed with sodium perchlorate. This test is to determine whether in addition to the normal pump function there is also normal organification. The dosage of sodiumperchlorate is 10 mg/kg body weight i.v., or: children up to 1 year 100 mg, 1-2 years 200 mg, 2-4 years 400 mg, adults 600 mg. Intravenous administration is indicated due to standardized time intervals for the "wash-out" images. Additional measurements are made 30 and 60 min after the administration of perchlorate.  
Attention: sodium perchlorate is not registered for this (i.v.) route of administration and indication.

## 11. Interpretation

- a. Interpretation of the scintigram requires knowledge of the physiology and pathophysiology of the thyroid gland. Diffusely increased uptake in the thyroid gland is observed in Graves' disease and in secondary hyperthyroidism, such as a TSH-producing pituitary tumour (rare) or a molar pregnancy (hydatidiform mole) (very rare). A toxic nodule or toxic multinodular goitre will show (multi)focally increased uptake. In such instances the uptake in normal thyroid tissue is more or less suppressed. Thyrotoxicosis with reduced uptake in the thyroid gland is seen in thyroiditis (possibly partial, rarely unilateral), in thyrotoxicosis factitia, and in struma ovarii (very rare).
- b. Where vital follicular cells are absent, cold regions develop. There are many causes for this (cysts, haemorrhage, hypo- or afunctional adenoma, carcinoma). Iodine uptake is generally absent or clearly reduced in a malignant lesion. This becomes visible on the scintigram if the diameter of the abnormality is at least 0,5-1 cm. In exceptional cases (3-8%) there is a discrepancy between imaging with pertechnetate and with iodine. This occurs when the follicular cells in a nodule still have access to the iodine

pump (NIS) but organification no longer takes place. Such a finding may indicate a malignancy. The opposite, though very rare, has also been described: malignancy depicted as a cold nodule with pertechnetate and as a hot nodule with iodine. In principle, however, <sup>99m</sup>Tc-pertechnetate scintigraphy is insufficient. When a solitary nodule is 'cold', it is advisable to proceed to a fine-needle aspiration biopsy (FNA), except if the nodule forms part of a long-standing multinodular goitre, which does not feel solid and has undergone no recent growth. A nodule with iso-intense uptake as compared to the surrounding thyroid tissue should be treated as a cold nodule.

- c. Neonates normally also have a butterfly-shaped thyroid gland located just above the suprasternal notch. In the case of congenital or prolapse disorders, thyroid tissue may be observed at the base of the tongue. An organification disorder is diagnosed if a reduction of  $\geq 20\%$  of the activity in the thyroid is ascertained 30 min post i.v. administration of sodium perchlorate. When the decrease in activity is 10-20% , the result is equivocal. This 'wash-out test' is not carried out until at least 4 h after the administration of the <sup>123</sup>I sodium iodide.
- d. Recent administration of iodinated compounds, such as x-ray contrast or iodinated medication, interferes with thyroid gland diagnostics because of competition between the uptake of the radiopharmaceutical and cold iodine (see also Section 9. Patient Preparation).

## 12. Report

Size, shape and location of the thyroid as well as the distribution of the radiopharmaceutical within this gland are described in relation to the findings upon palpation. The volume of the thyroid estimated by palpation and/or calculated scintigraphically, is stated in the report. The scintigraphically calculated volume remains an estimation, it is not a precise measurement. It is important to realise this when calculating the therapeutic dose of <sup>131</sup>I in Graves' disease (see section 5. Relation to other diagnostic procedures / therapies). For <sup>123</sup>I-scintigraphy, the image is described and the iodine uptake as a percentage of the administered dose is reported.

## 13. Literature

- ACR–SNM–SPR Practice Guideline For The Performance Of Thyroid Scintigraphy And Uptake Measurements. October 1, 2009.
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